NPS Snapshot:

Orphines

HISTORY AND KEY DATES

A new wave of synthetic opioids, distinct from fentanyl and its analogs, is emerging in forensic samples. Also known as piperidinylbenzimidazolones, these novel synthetic opioids now referred to as orphines were initially developed for their anesthetic and antitussive properties.

1960s

Janssen Pharmaceutica patents a series of potent, morphine-like benzimidazolinyl piperidines.

2018

Substituted *N*-benzyl piperidine 4-benzimidazolones, including brorphine, are studied for their μ-opioid receptor activity in a *Journal of Medicinal Chemistry* paper.

2019

Brorphine is reported to the United Nations Office on Drugs and Crime (UNODC) Early Warning Advisory on NPS.

July 2020

Brorphine was first identified in the United States.

January 2021

Brorphine was placed into emergency Schedule I by the US Drug Enforcement Administration (DEA).

March 2022

Brorphine was placed under international control by the United Nations Commission on Narcotic Drugs (CND).

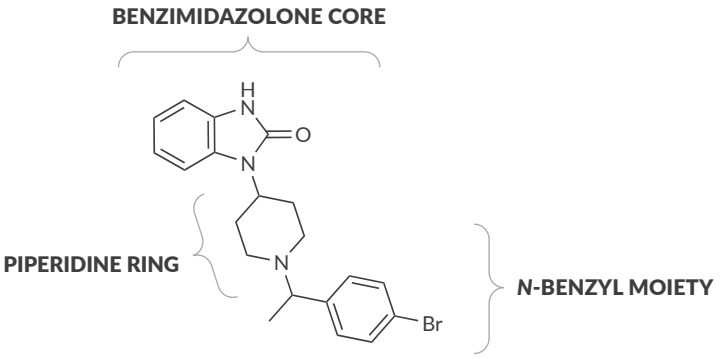
2024

Four orphine analogs were reported for the first time to the UNODC Early Warning Advisory on NPS.

2025

Spirochlorphine (R-6890) is first reported to the UNODC Early Warning Advisory on NPS.

PROTOTYPICAL STRUCTURE



PHARMACOLOGY

In vitro data from Vandeputte, *et al.*, 2024 show that brorphine and its related analogs have high affinity for the μ-opioid receptor and act as agonists. Fluorphine, chlorphine, and brorphine induced pronounced respiratory depression. Notably, the study found that naloxone may not fully reverse the respiratory depression induced by some of these compounds.

More Than 15 Orphine Analytical Standards Available:

- Metabolites
- Isotopically Labeled Standards
- DEA Exempt Preparations
- CRMs

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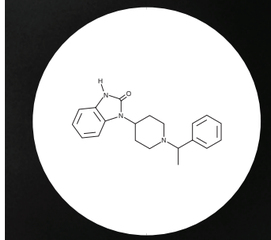
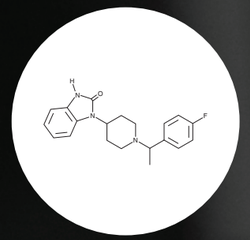
AVAILABLE ORPHINE ANALYTICAL STANDARDS

Classic Orphine NPS

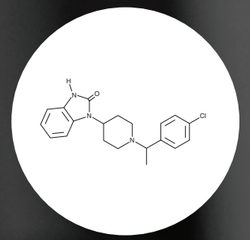
Contain a benzimidazolone core, a piperidine ring system, along with an *N*-benzyl moiety. These structural features may or may not have additional substituents/modifications. Metabolites may have a truncated scaffold.



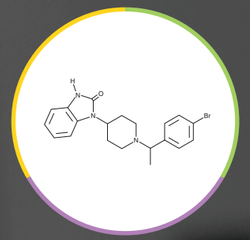
Orphine
(36303)



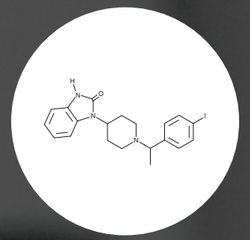
Fluorphine
(36302)



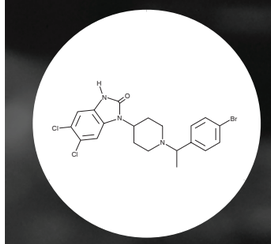
Chlorphine
(36301)



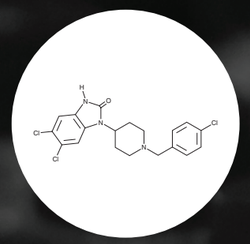
Brorphine
(34184 | 27816 | 31566 | 38145)



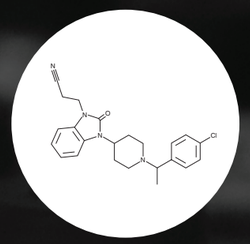
Iodorphine
(37062)



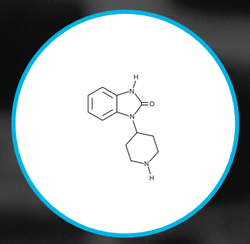
5,6-dichloro Brorphine / SR-14968
(40532)



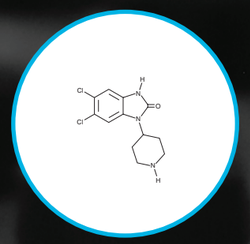
SR-17018 / 5,6-dichloro Desmethylchlorphine
(24480)



N-Propionitrile Chlorphine / Cychlorphine
(40326)



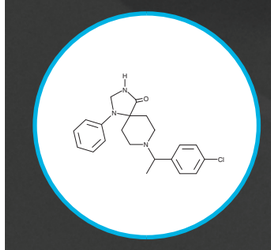
nor-Orphine / N-desalkyl Orphine
(37339)



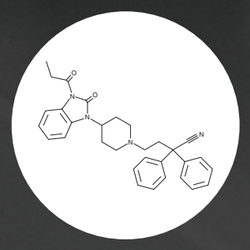
5,6-dichloro nor-Orphine
(43170)

Orphine-Related NPS

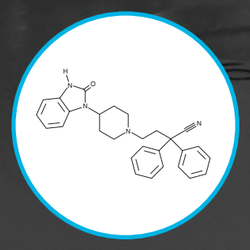
Fall outside the prototypical scaffold but are closely related in terms of structure and pharmacology, including spirocyclic and phenethyl analogs.



R-6890 / Spirochlorphine
(39967)



Bezitramide / R-4845
(42345)



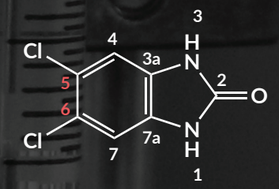
Despropionyl Bezitramide / R-4618
(43337)

Metabolite or potential metabolite | CRM | Internal Standard | Exempt Preparation

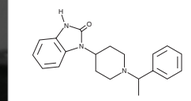
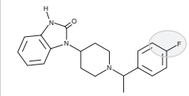
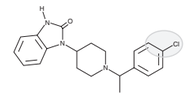
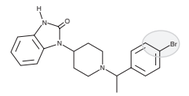
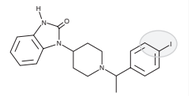
Navigating Orphine Naming Conventions

Classic orphine NPS follow the legacy naming of **brorphine**, substituting the **bror-** prefix for the corresponding halogen substituent. Substituting bromine for fluorine yields *fluorphine*, the chlorine analog is referred to as *chlorphine*, and the iodine analog *iodorphine*. The unsubstituted analog is simply referred to as *orphine*.

Additionally, 5,6-dichloro compounds are named based on the numbering system around the benzimidazolone core.

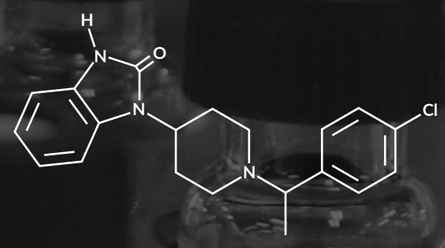


5,6-dichloro compound naming

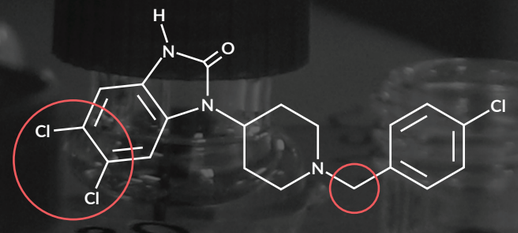
					
Substituent	None	Fluorine	Chlorine	Bromine	Iodine
Compound Name	Orphine	**Fl**uorphine	**Ch**lorphine	**Br**orphine	**Iod**orphine

For orphine NPS, we have aligned the naming of their synonyms to create a bridge between legacy lab codes named in scientific literature and the orphine scaffold.

For example, one can think of SR-17018 as 5,6-dichloro desmethylchlorphine. It contains the chlorphine scaffold but lacks the methyl group at the benzyl location and has two chlorine substituents at the 5- and 6-positions on the benzimidazolone.



Chlorphine



SR-17018 / 5,6-dichloro Desmethylchlorphine

FORENSIC TOOLS & RESOURCES FOR NPS IDENTIFICATION

Cayman Chemical is dedicated to working with the forensic community to quickly make authentic reference standards available from our ISO/IEC 17025 and ISO 17034 laboratories. Cayman offers many free resources to assist the forensic community in the screening and identification of unknown substances.

NPS DASHBOARD

We collaborate with the Center for Forensic Science Research & Education (CFSRE) to provide analytical reference standards for emerging NPS. Cayman maintains an updated dashboard to align with the CFSRE's quarterly NPS scope recommendations, matching reference standards with recommended NPS to help testing laboratories easily find reference standards to the most pressing NPS.

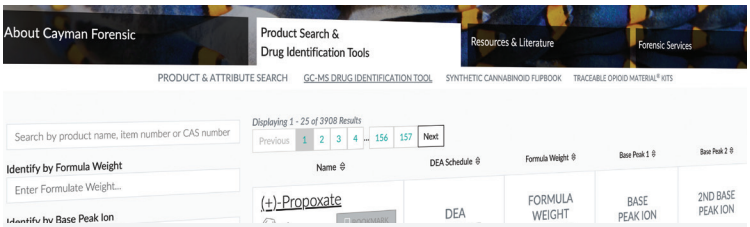
View the dashboard at **www.caymanchem.com/NPS-dashboard**

MASS SPEC RESOURCES

Cayman Spectral Library

Our free, searchable, GC-MS spectral database contains 70eV EI mass spectral data of 2,500+ of Cayman's forensic drug standards.

Download the database at **www.caymanchem.com/CSL**



GC-MS Drug Identification Tool

Cayman's GC-MS drug identification tool can help you search unknowns by formula weight, base peak, and 2nd base peak ion.

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